# Literature Report IX

## Iridium Nitrenoid-Enabled Arene C−H Functionalization

**Reporter: Jian Chen**
**Checker: Kai Xue**
**Date: 2024-09-23**

Qi, L.-W.; Rogge, T.; Houk, K. N.; Lu, Y. *Nat. Catal.* **2024**, *7*, 934-943

# CV of Prof. Lu Yixin

## Research:

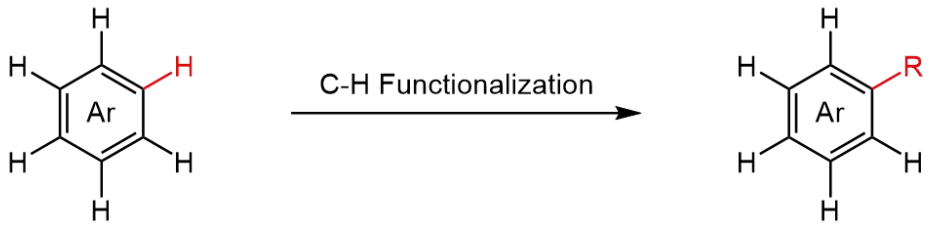
- Asymmetric catalysis and synthesis
- Transition metal catalysis
- Photoredox catalysis
- Sustainable chemistry

## Background:

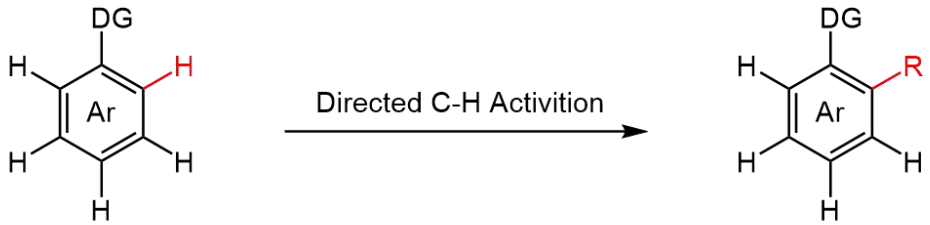
- **2000** Ph.D., McGill University
- **2000-2003** Postdoc., Clinical Research Institute of Montreal; Nagoya University
- **2003-Now** Professor, National University of Singapore

# Contents

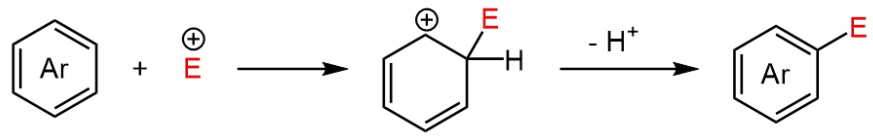
# Introduction




**Natural product** synthesis
Late-stage **drug molecule** functionalization

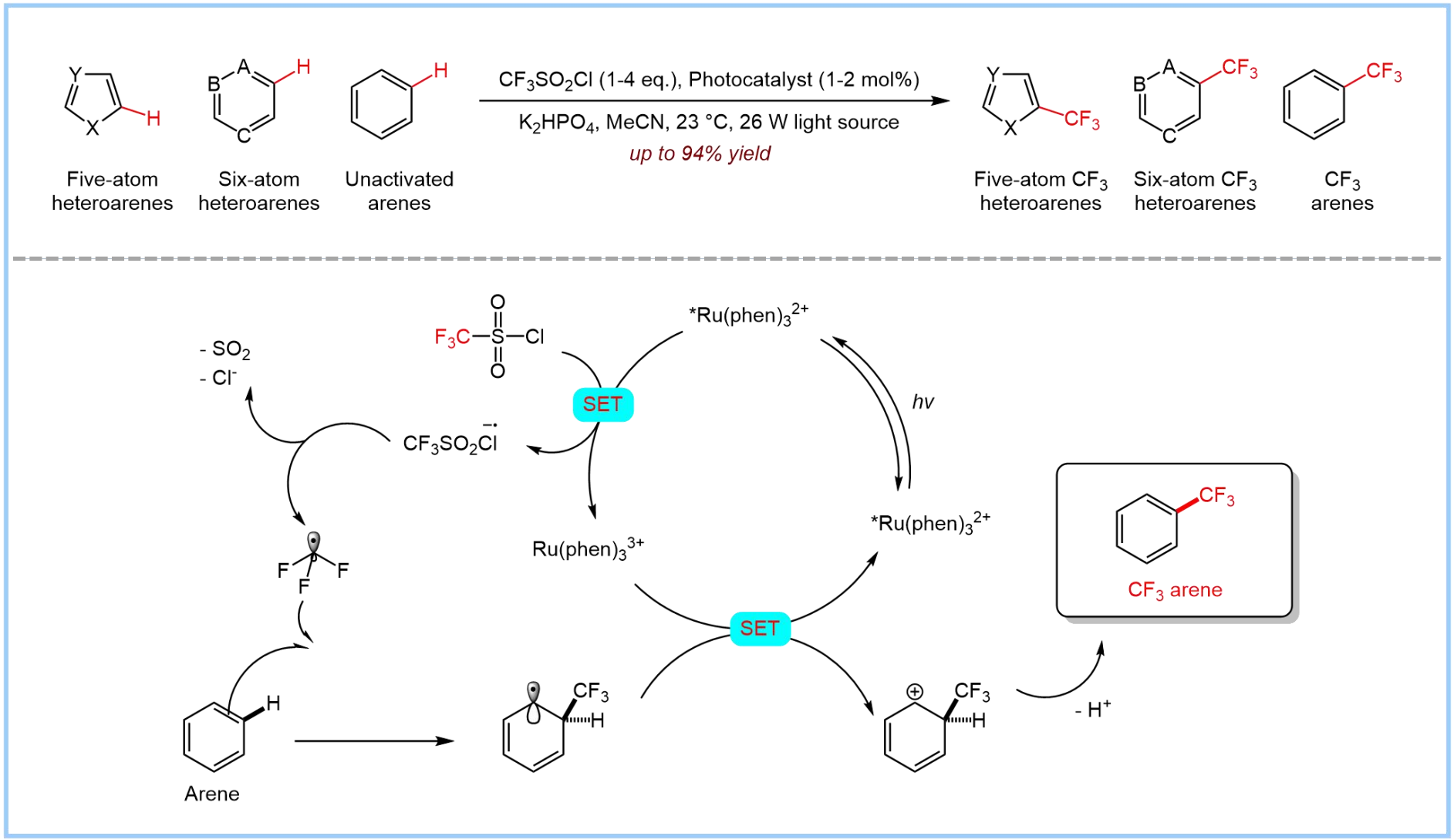



Engagement of a **directing group**
Judicious selection of a **metallic catalytic system**



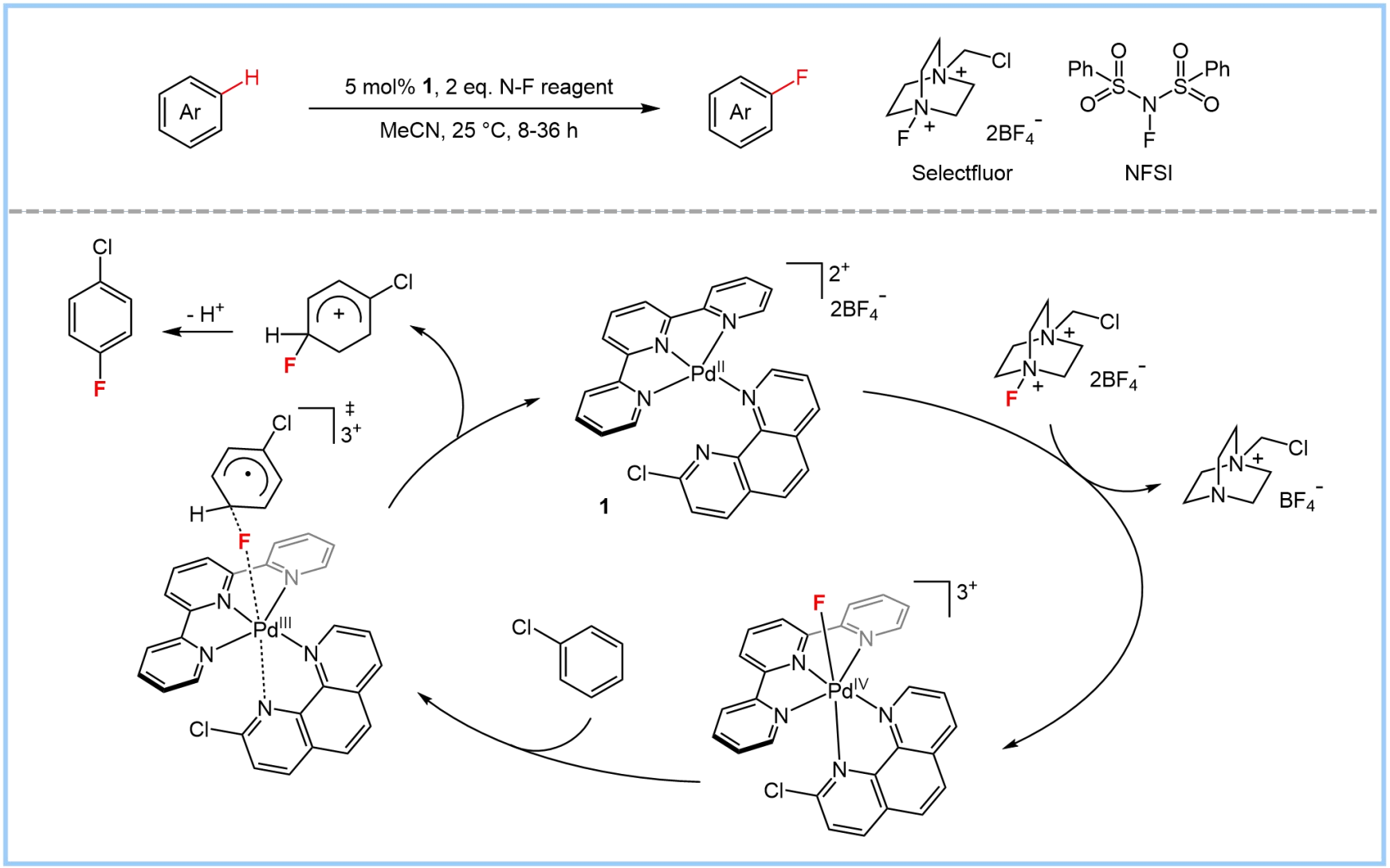

**The most common** reaction type for arenes including **fluorination**, **thianthrenation**, **borylation**, and **trifluoromethylation**

# Introduction



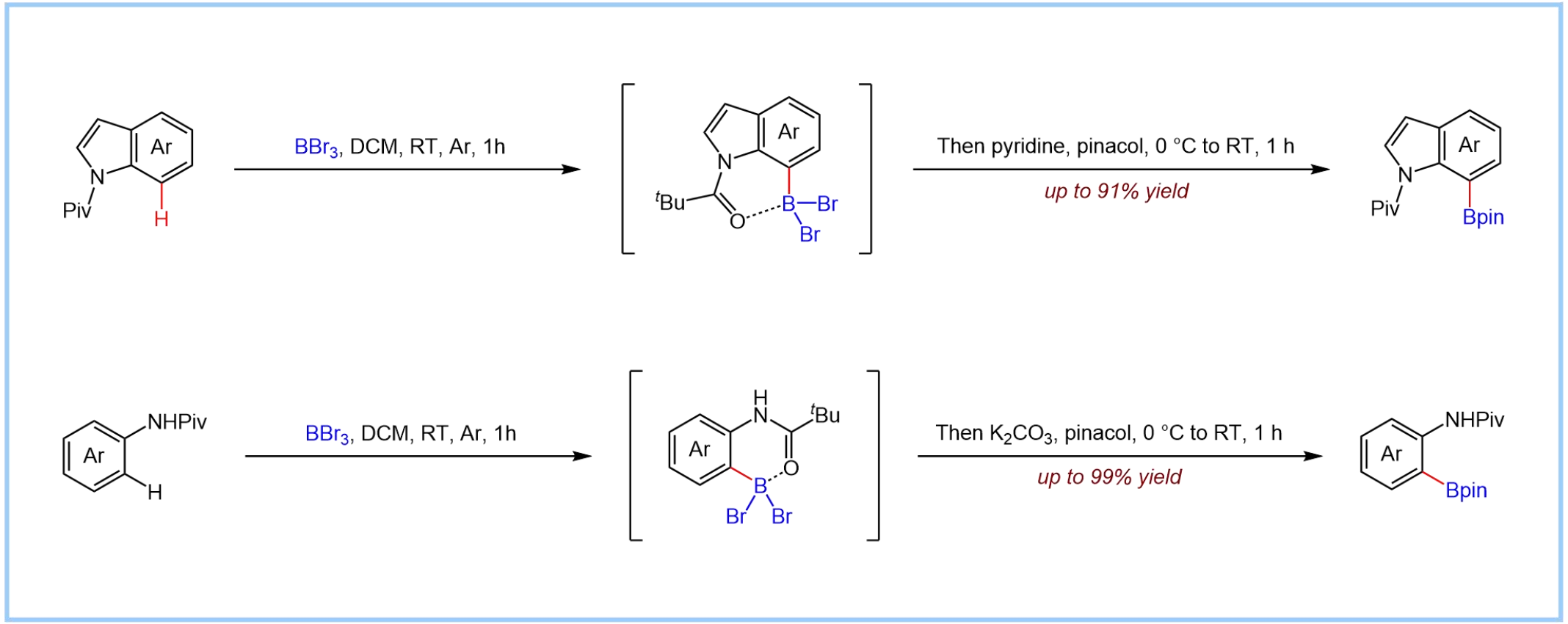

Nagib, D. A.; MacMillan, D. W. C.* *Nature* **2011**, *480*, 224

# Introduction



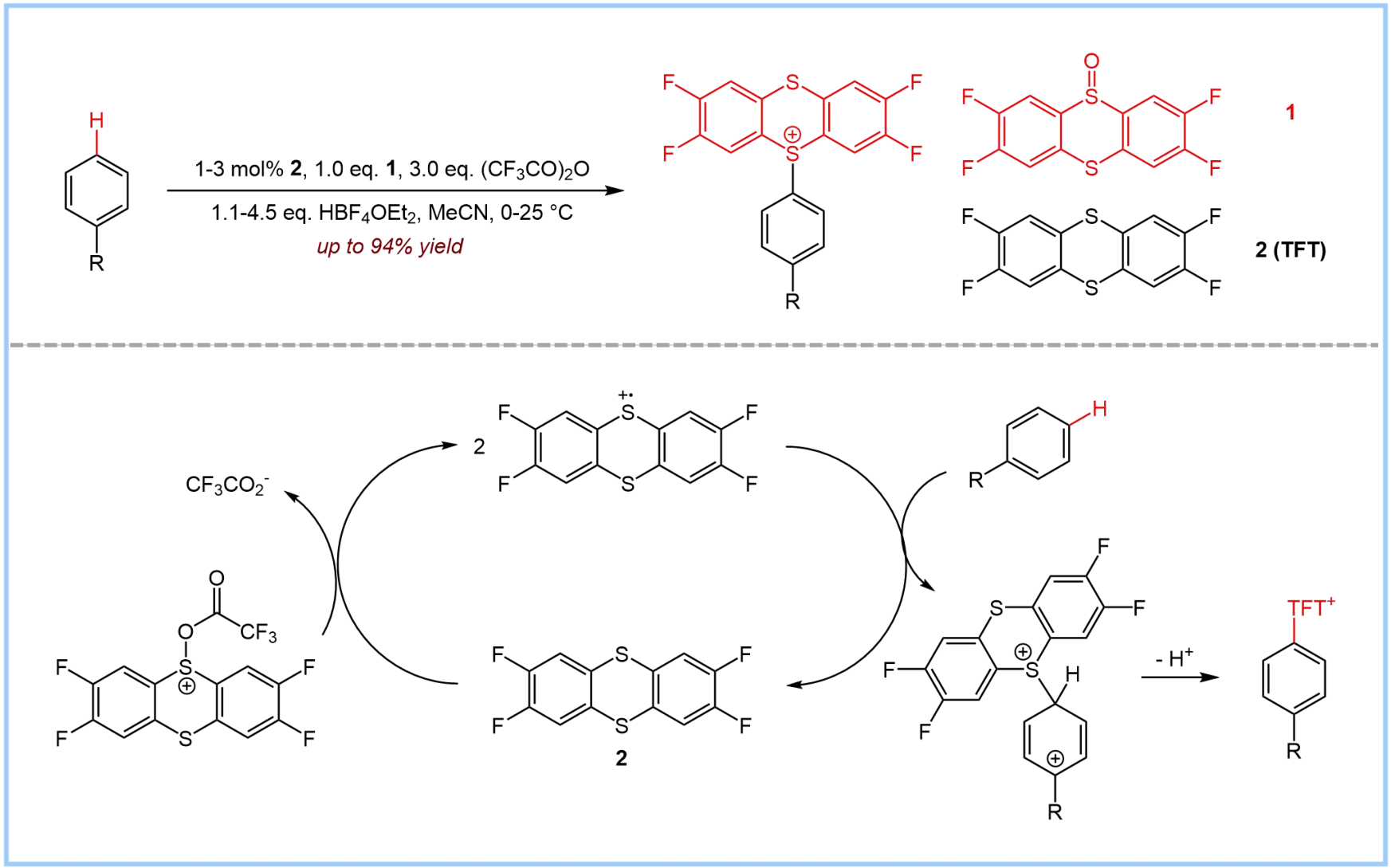

Yamamoto, K.; Li, J.; Garber, J. A. O.; Ritter, T.* *Nature* **2018**, *554*, 511

# Introduction



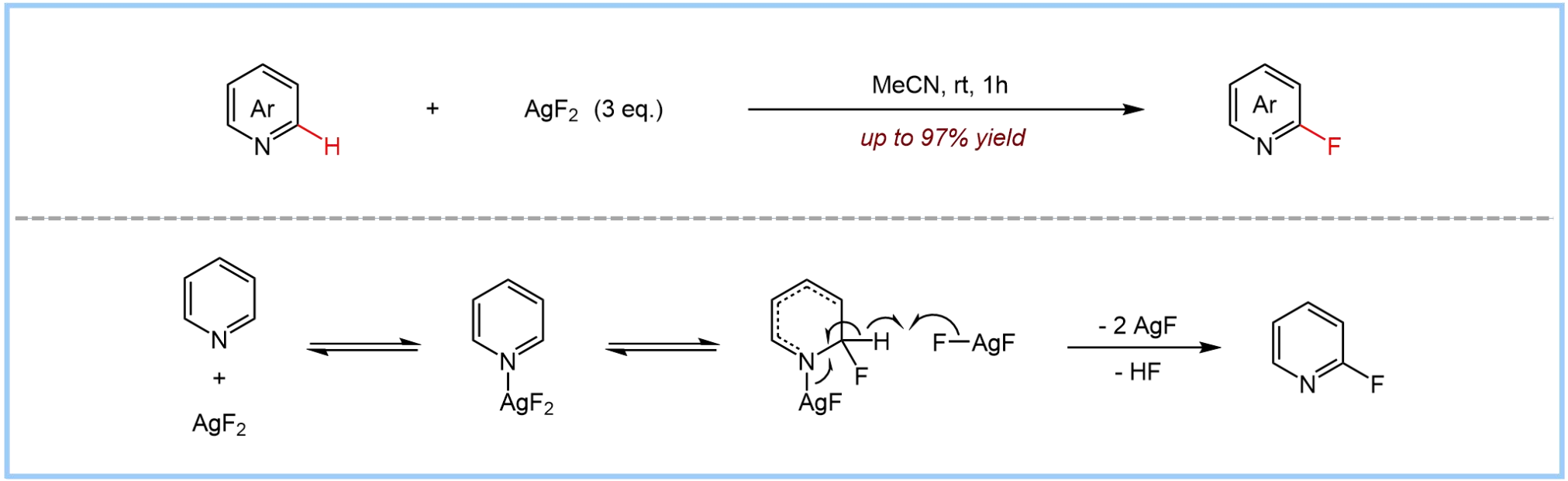

Lv, J.; Chen, X.; Xue, X.-S.; Shi, Z.* *Nature* **2019**, *575*, 336

# Introduction



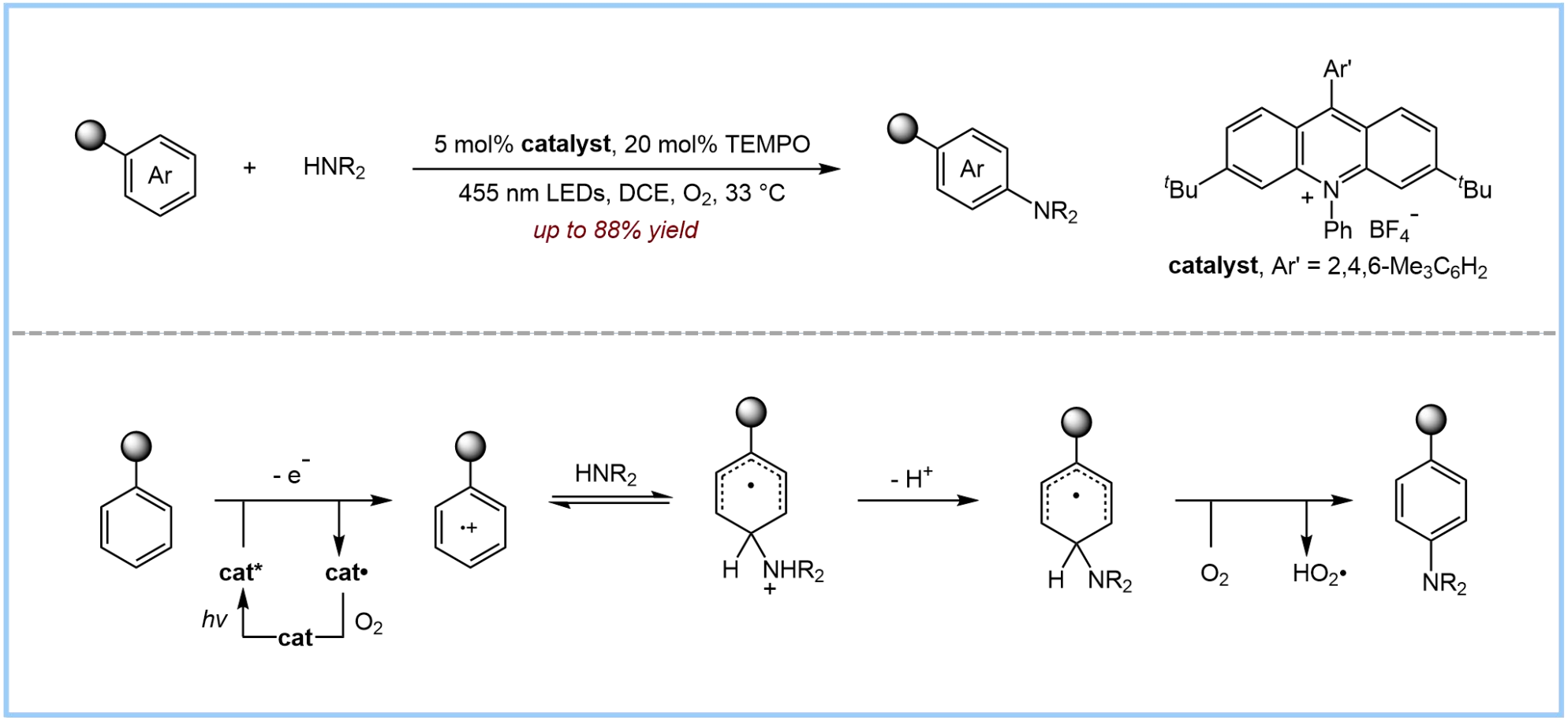

Berger, F.; Plutschack, M. B.; Riegger, J.; Ritter, T.* *Nature* **2019**, *567*, 223

# Introduction



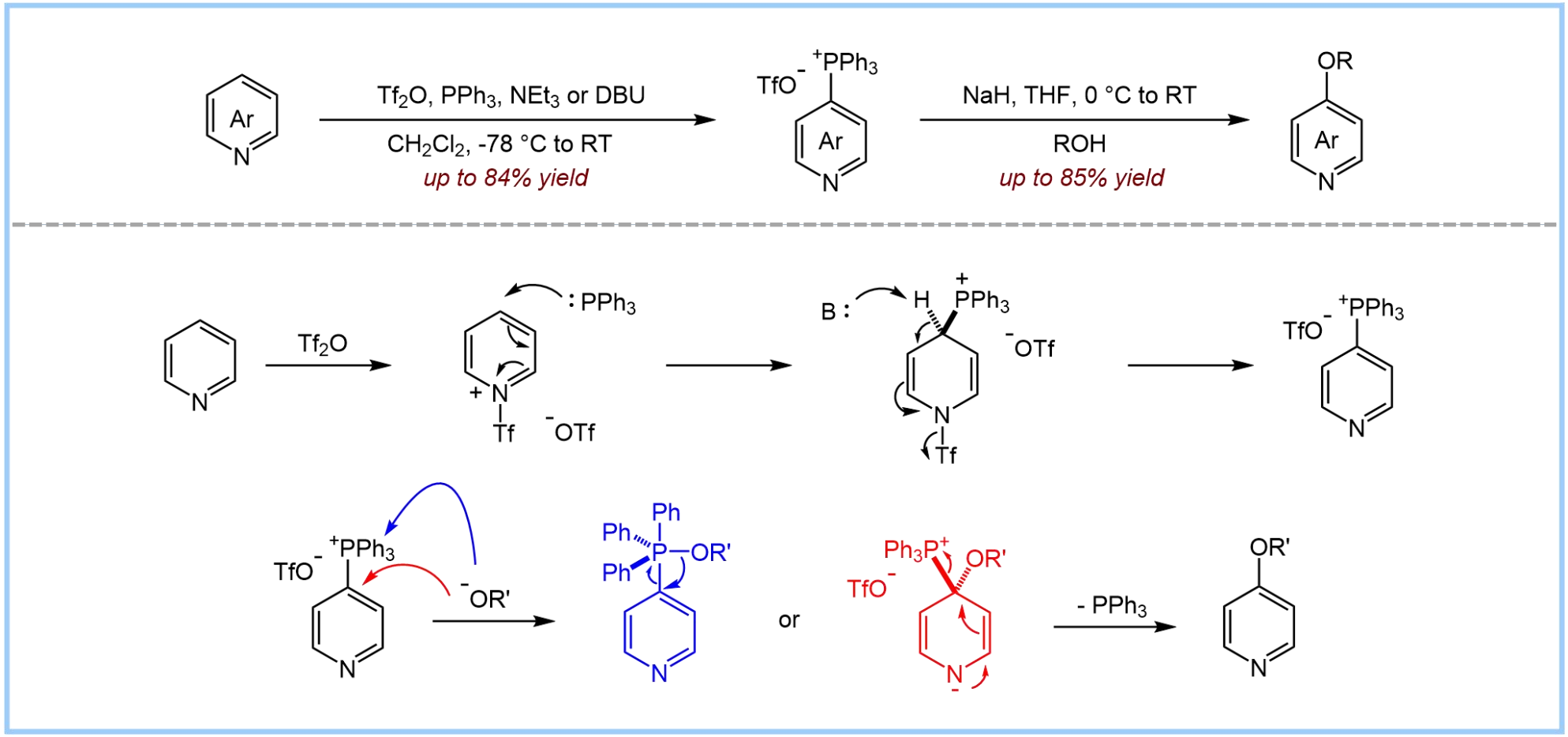

Fier, P. S.; Hartwig, J. F.* *Science* **2013**, *342*, 956

# Introduction




Romero, N. A.; Margrey, K. A.; Nicewicz, D. A.* *Science* **2015**, *349*, 1326

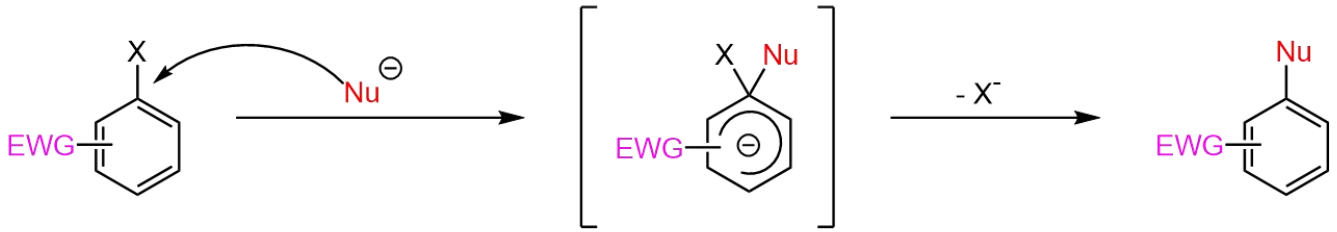
# Introduction



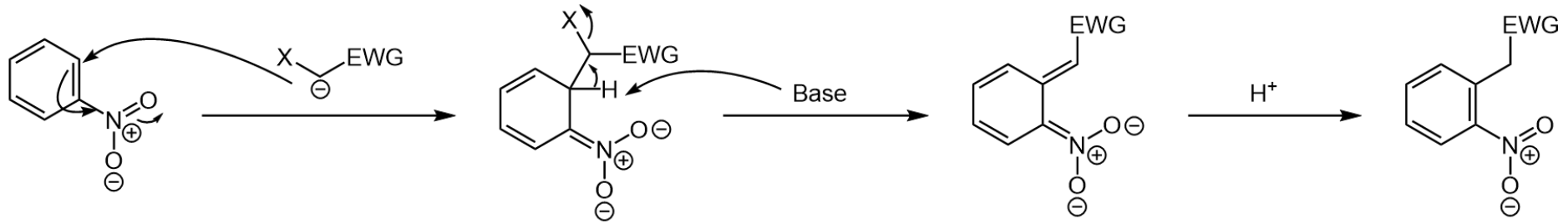

Hilton, M. C.; Dolewski, R. D.; McNally, A.* *J. Am. Chem. Soc.* **2016**, *138*, 13806

# Introduction

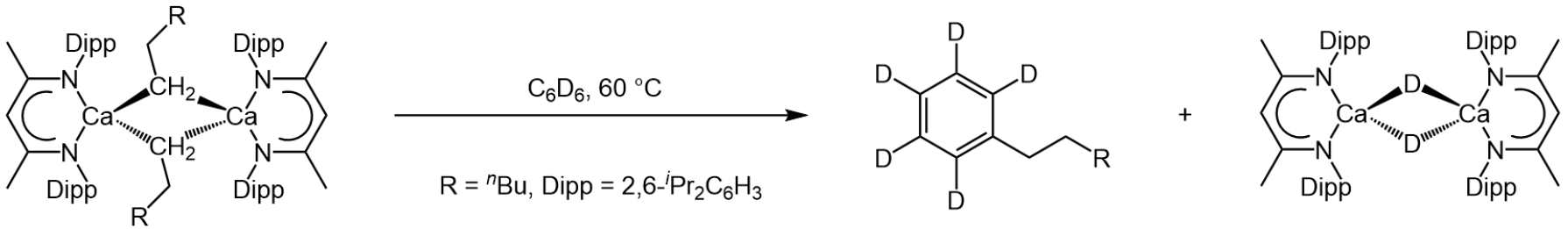
**$S_NAr$**




**Vicarious Nucleophilic Substitution**



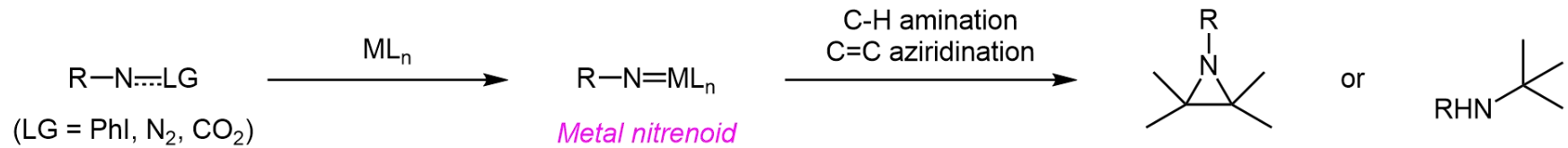
# Introduction



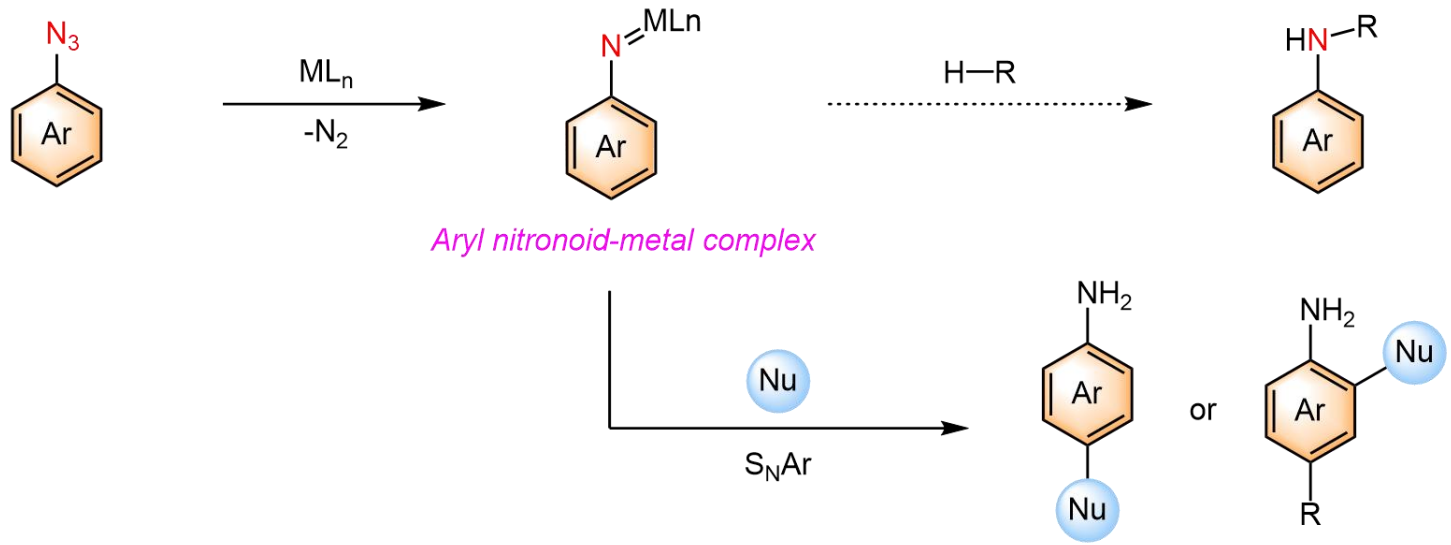

Wilson, A. S. S.; Hill, M. S.; Mahon, M. F.; Mahon, L.* *Science* **2017**, *358*, 1168

# Project Synopsis

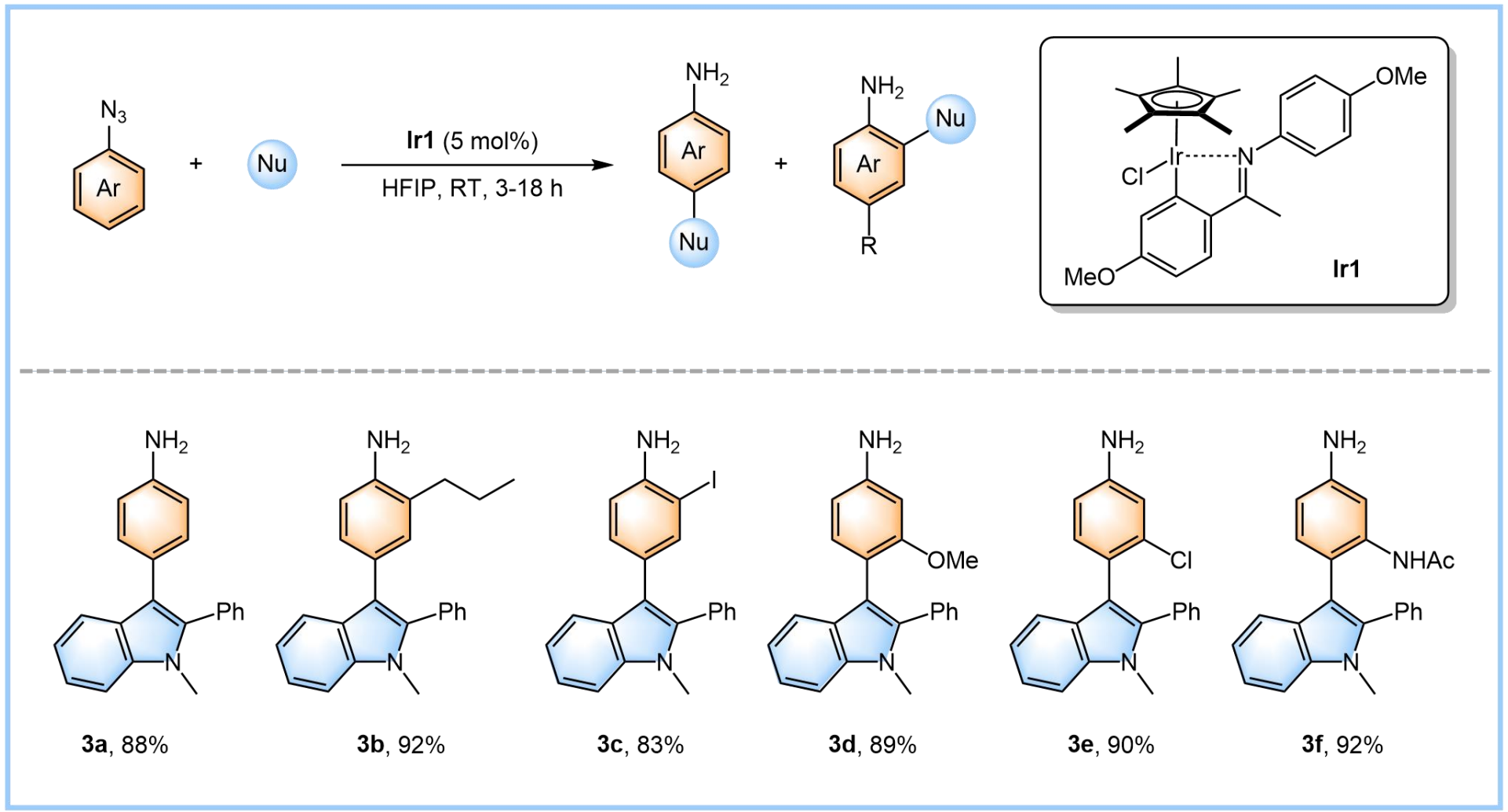
**Nitrene transfer reactions**



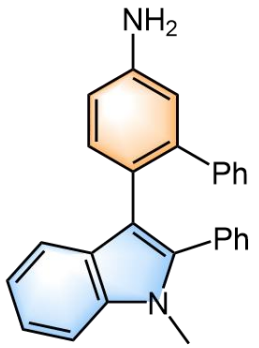

**This work**



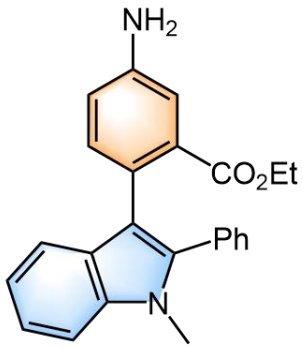
# Substrate Scope



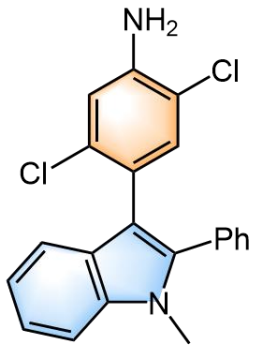
# Substrate Scope



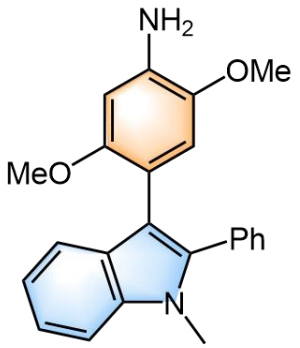

**3g**, 84%



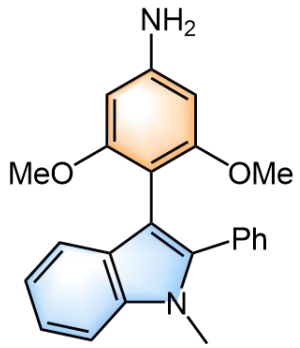

**3h**, 87%



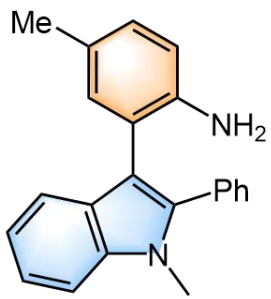

**3i**, 87%



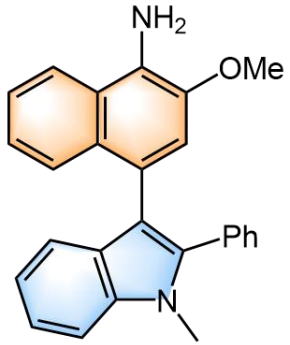

**3j**, 94%



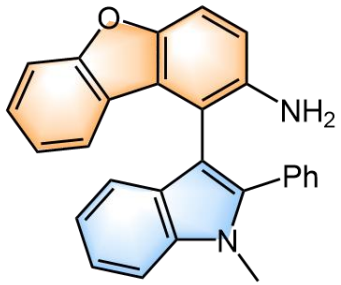

**3k**, 95%, (*p*/*o* = 8:1)



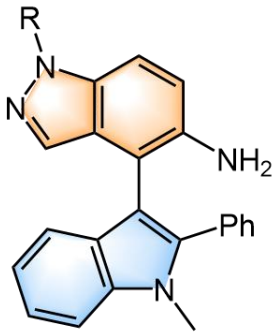

**3l**, 85%




**3m**, 87%

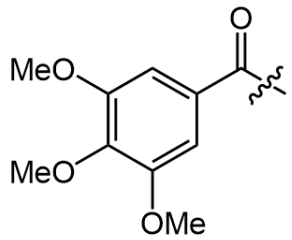



**3n**, 90%



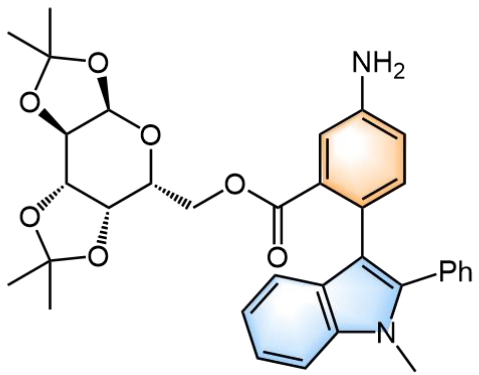

**3o**, 94%

R =

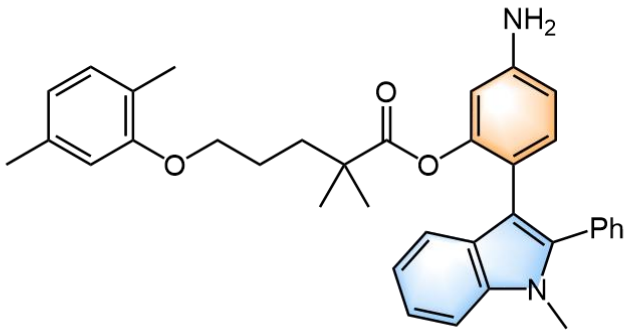



from MDG892

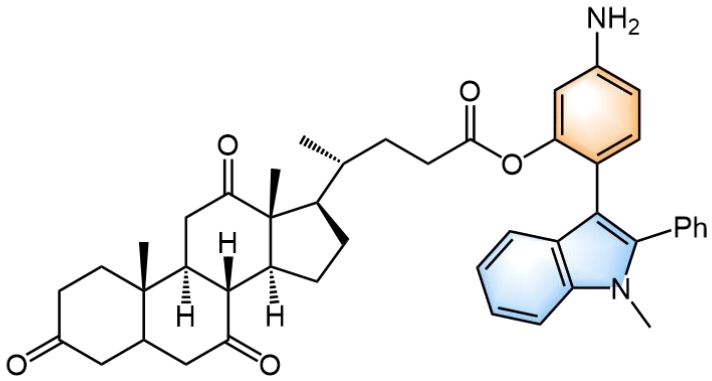
# Substrate Scope




**3p**, 82% (from D-galactose)

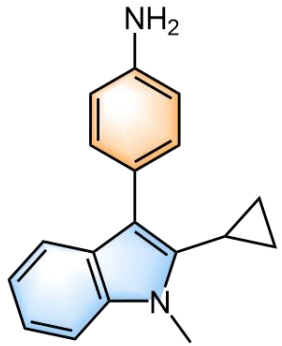



**3q**, 82% (from D-galactose)

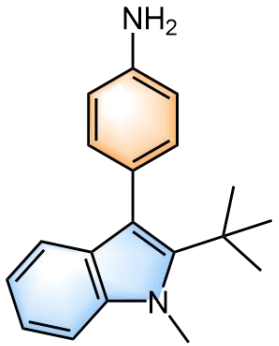



**3r**, 87% (from dehydrocholic acid)

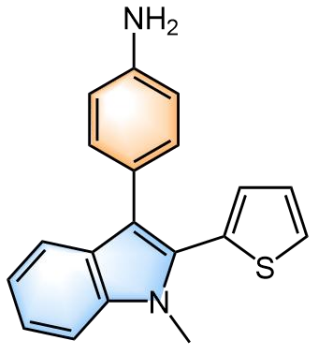
# Substrate Scope



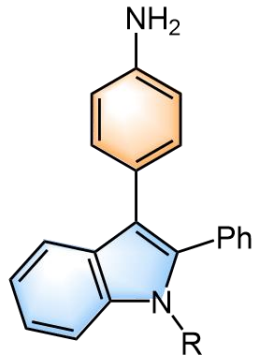

**3s**, 90%



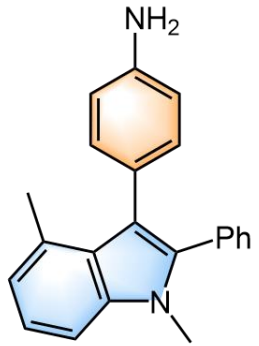

**3t**, 94%



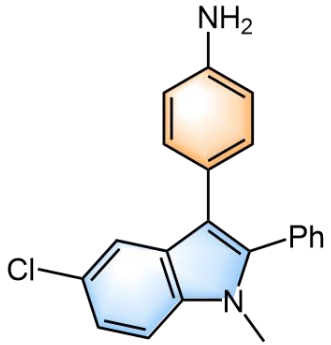

**3u**, 86%



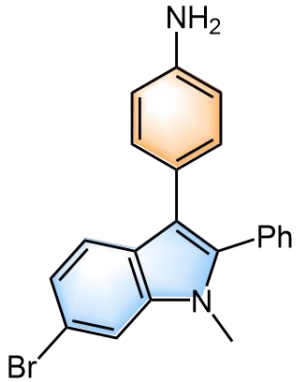

R = Bn, **3v**, 85% yield
R = $CO_2Me$, **3w**, NR



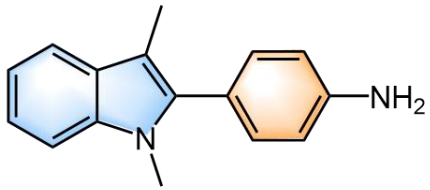

**3x,** 94%



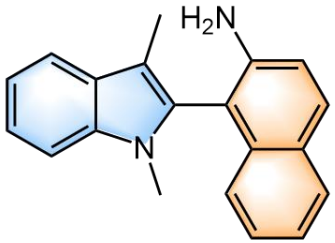

**3y,** 84%




**3z,** 82%

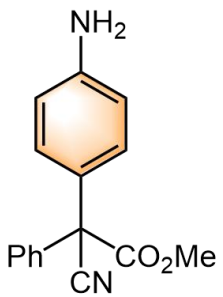



**3aa**, trace

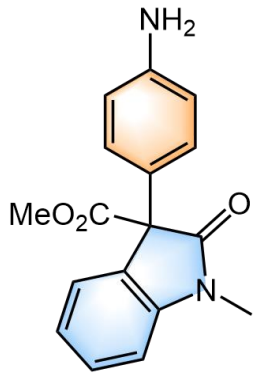



**3ab**, 72%

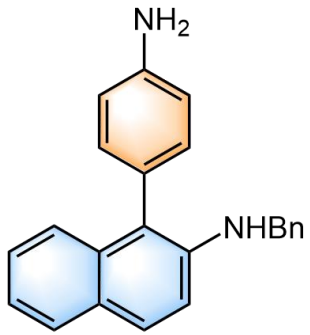
# Substrate Scope



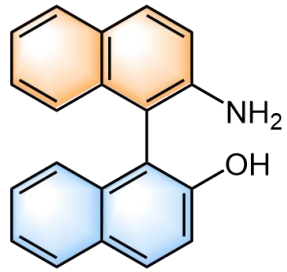

**4**, 93%




**5**, 98%

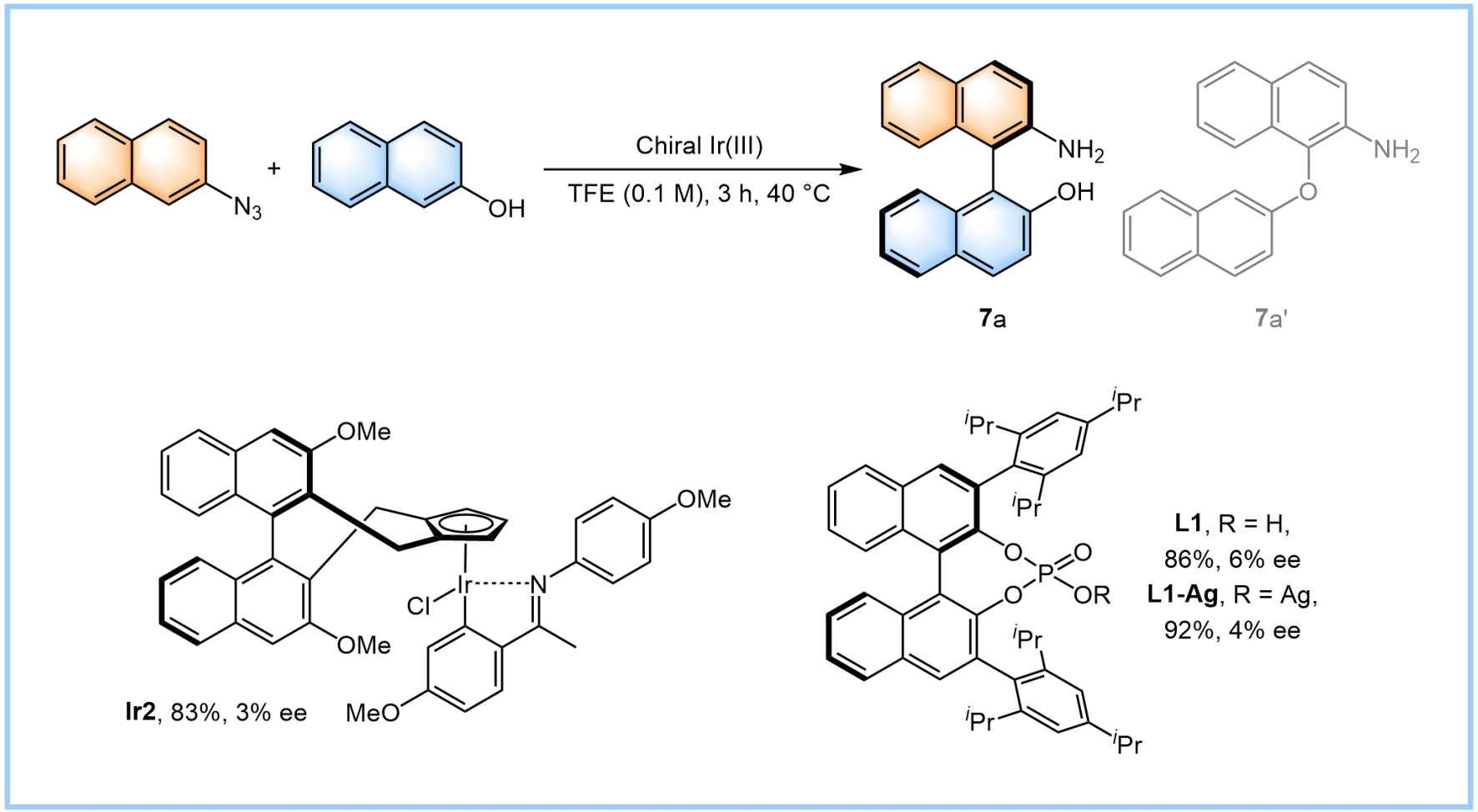



**6**, 88%

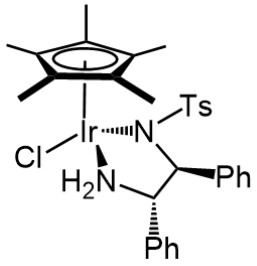



**7**, 92%

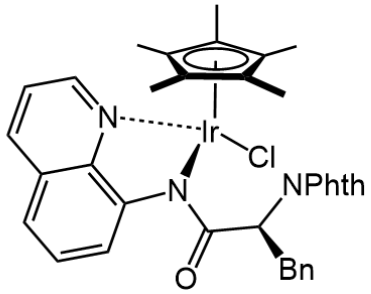
# Optimization of Reaction Conditions



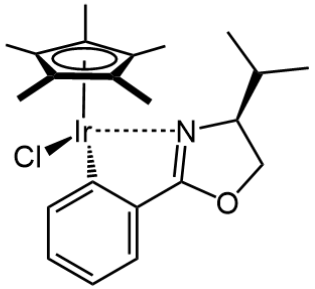
# Optimization of Reaction Conditions



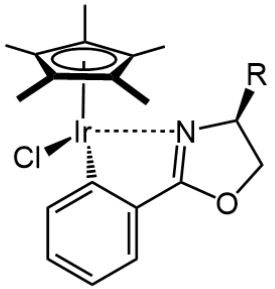

**Ir3**, NR



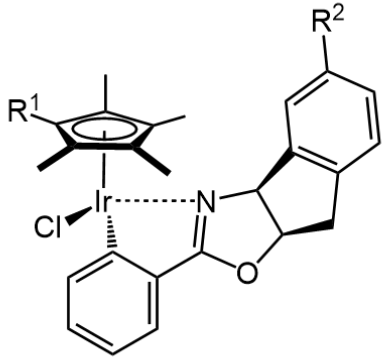

**Ir4**, trace



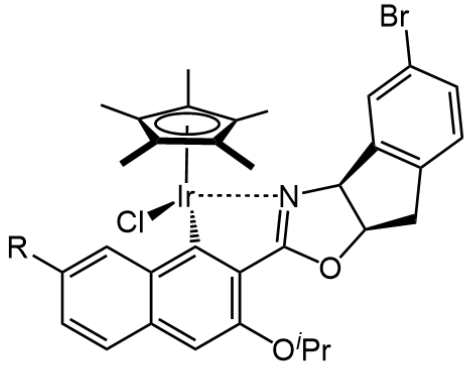

**Ir5**, 94%, 22% ee




**Ir6**, R = $^{t}$Bu, 94%, 6% ee
**Ir7**, R = Bn, 84%, 4% ee

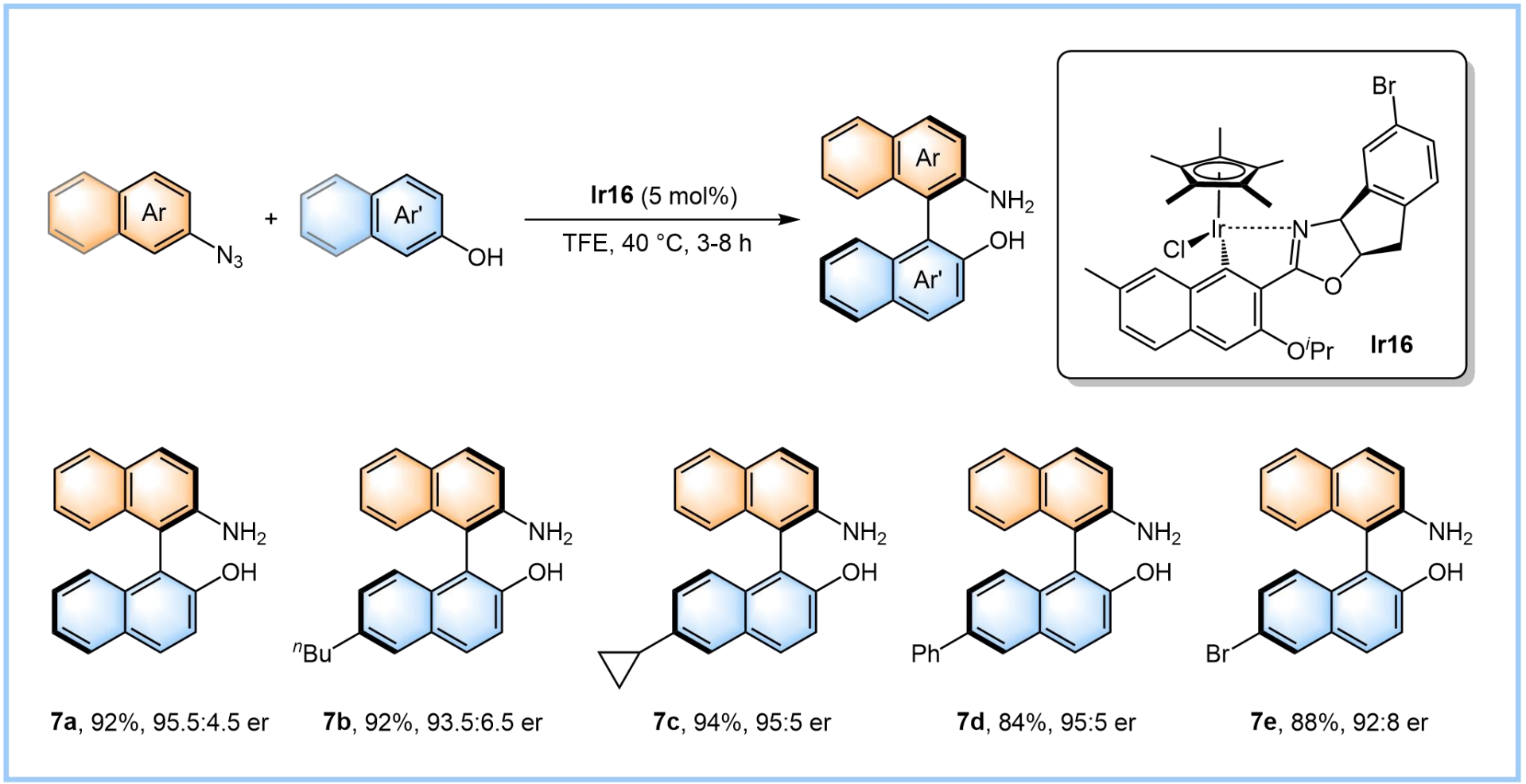



**Ir8**, $R^1$ = Me, $R^2$ = H, 92%, 50% ee
**Ir9**, $R^1$ = Ph, $R^2$ = H, 87%, 50% ee
**Ir10**, $R^1$ = $^{n}$Pr, $R^2$ = H, 88%, 42% ee
**Ir11**, $R^1$ = Me, $R^2$ = Br, 92%, 62% ee
**Ir12**, $R^1$ = Me, $R^2$ = Ph, 83%, 58% ee
**Ir13**, $R^1$ = Me, $R^2$ = 3,5-$Me_2C_6H_3$, 83%, 44% ee



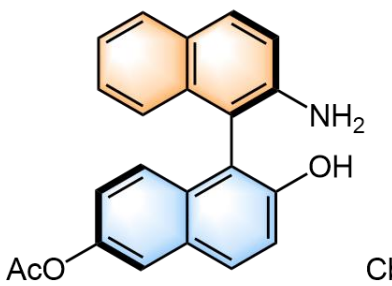

**Ir14**, R = H, 90%, 88% ee
**Ir15**, R = Br, 88%, 90% ee
**Ir16**, R = Me, 93%, 91% ee

# Substrate Scope

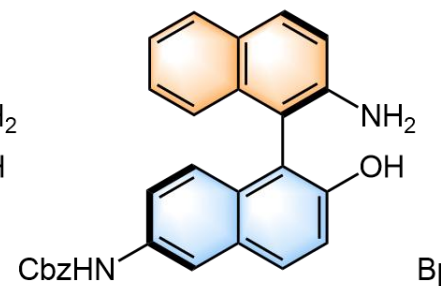



**7a**, 92%, 95.5:4.5 er **7b**, 92%, 93.5:6.5 er **7c**, 94%, 95:5 er **7d**, 84%, 95:5 er **7e**, 88%, 92:8 er

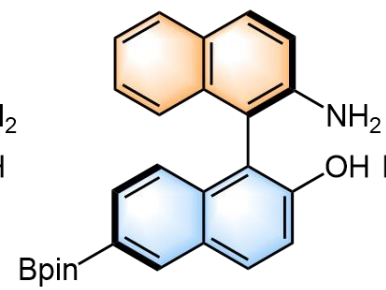
# Substrate Scope



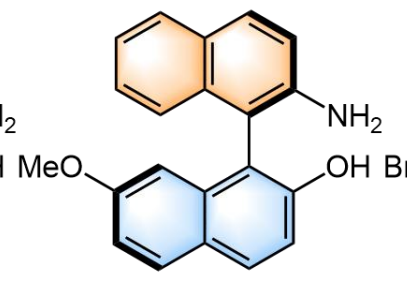

**7f**, 88%, 95.5:4.5 er



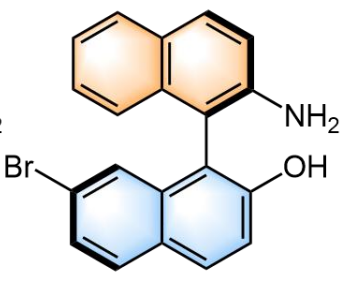

**7g**, 83%, 94:6 er



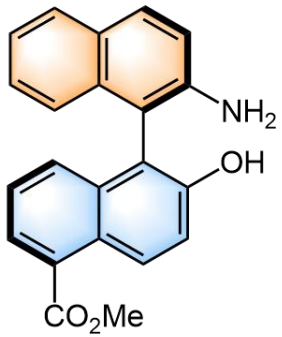

**7h**, 88%, 93.5:6.5 er



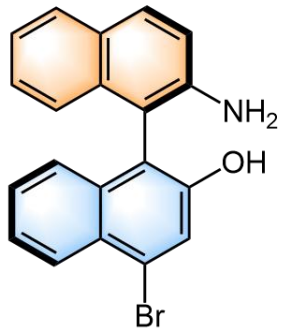

**7i**, 90%, 95:5 er



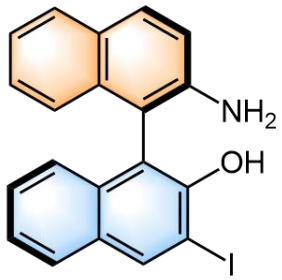

**7j**, 86%, 95:5 er



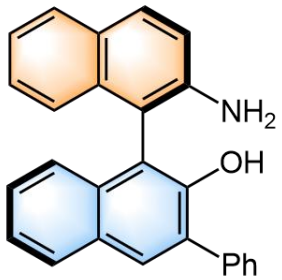

**7k**, 90%, 95:5 er



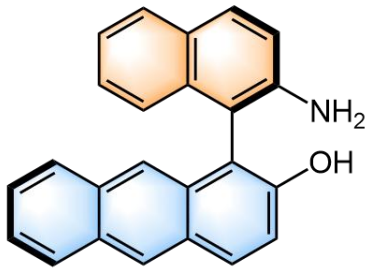

**7l**, 93%, 93.5:6.5 er




**7m**, 85%, 95:5 er

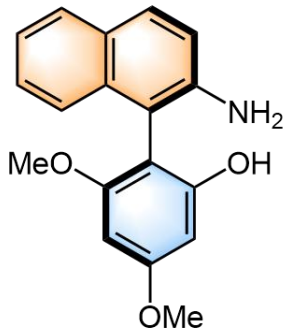



**7n**, 92%, 96:4 er

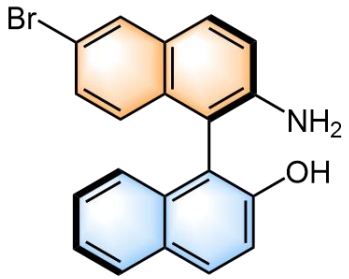



**7o**, 85%, 94:6 er

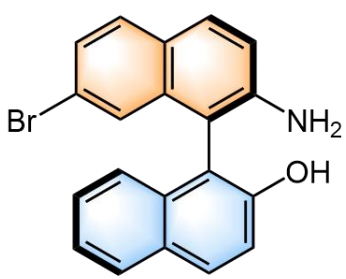
# Substrate Scope



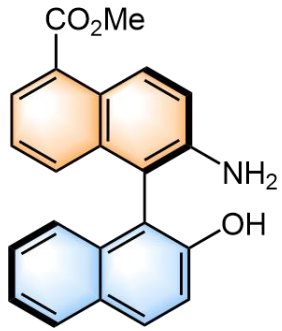

**7p**, 88%, 95.5:4.5 er



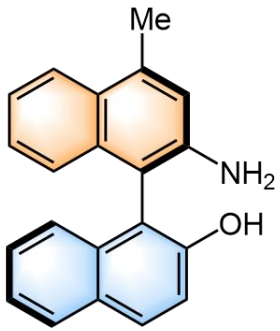

**7q**, 91%, 94.5:5.5 er



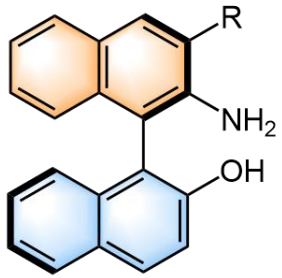

**7r**, 91%, 94.5:5.5 er



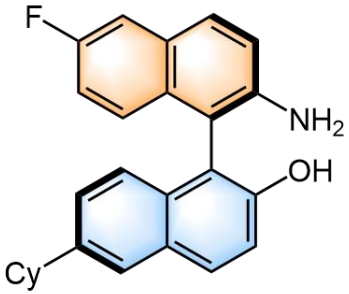

**7w**, 87%, 94:6 er



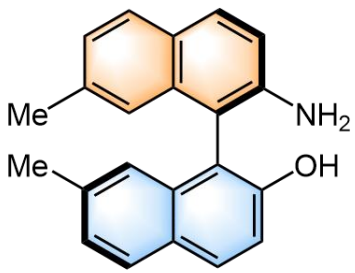

**7x**, 94%, 95:5 er



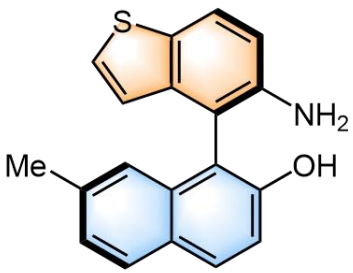

**7y**, R = Me, trace
**7z**, R = I, NR



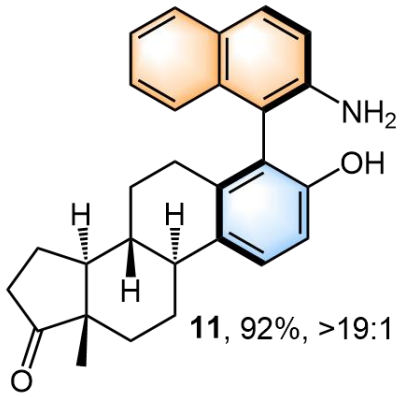

**8**, 90%, 97:3 er




**9**, 90%, 97:3 er

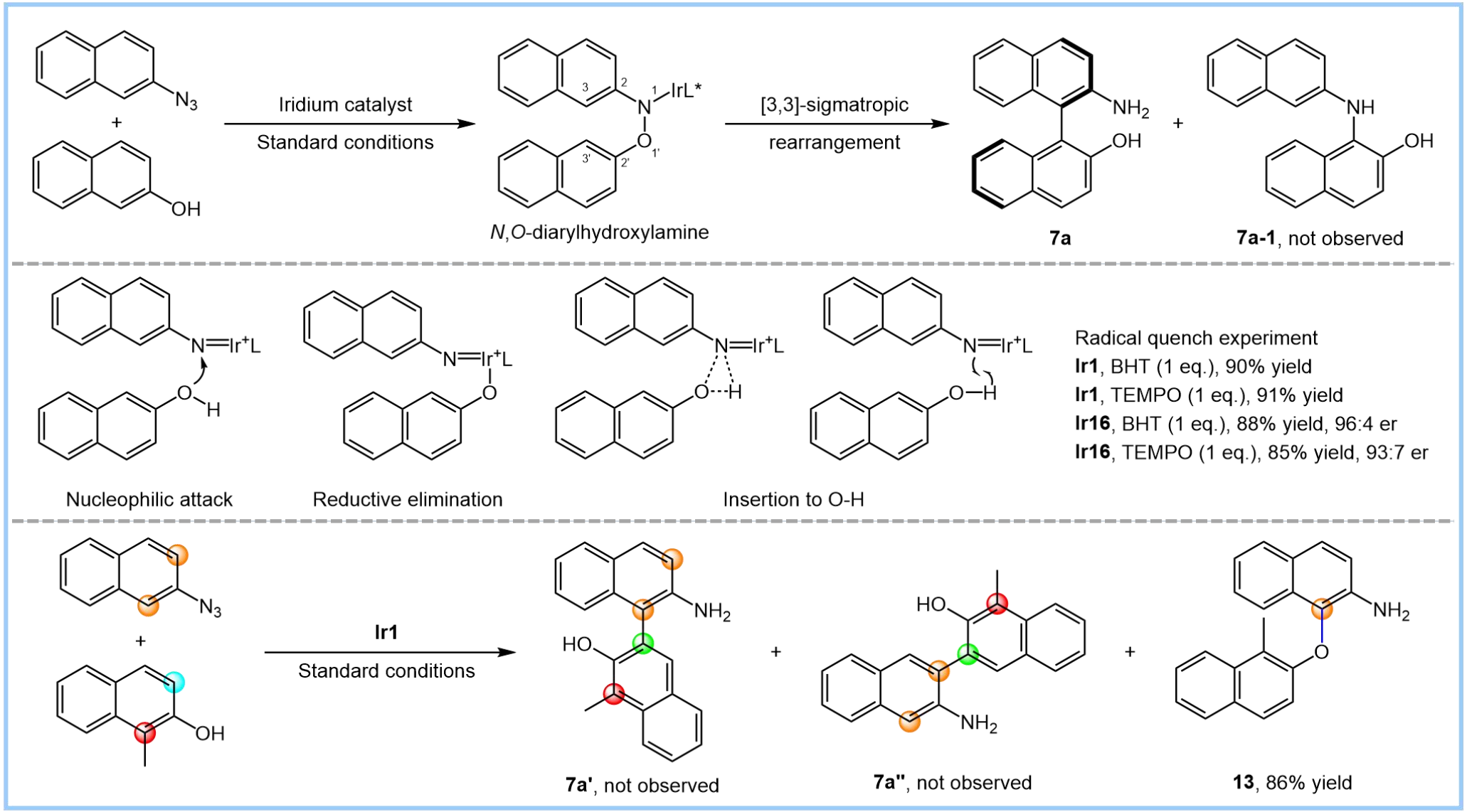



**10**, 90%, 97:3 er

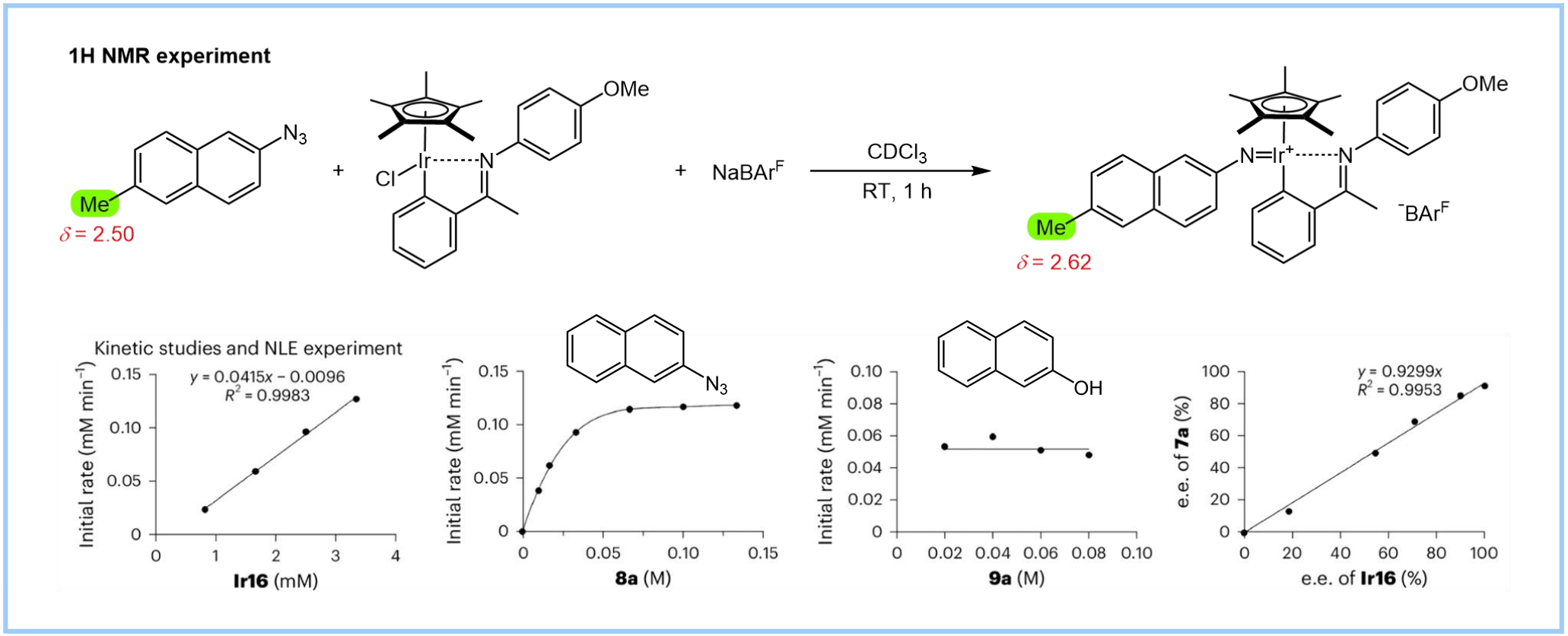



**11**, 92%, >19:1 dr

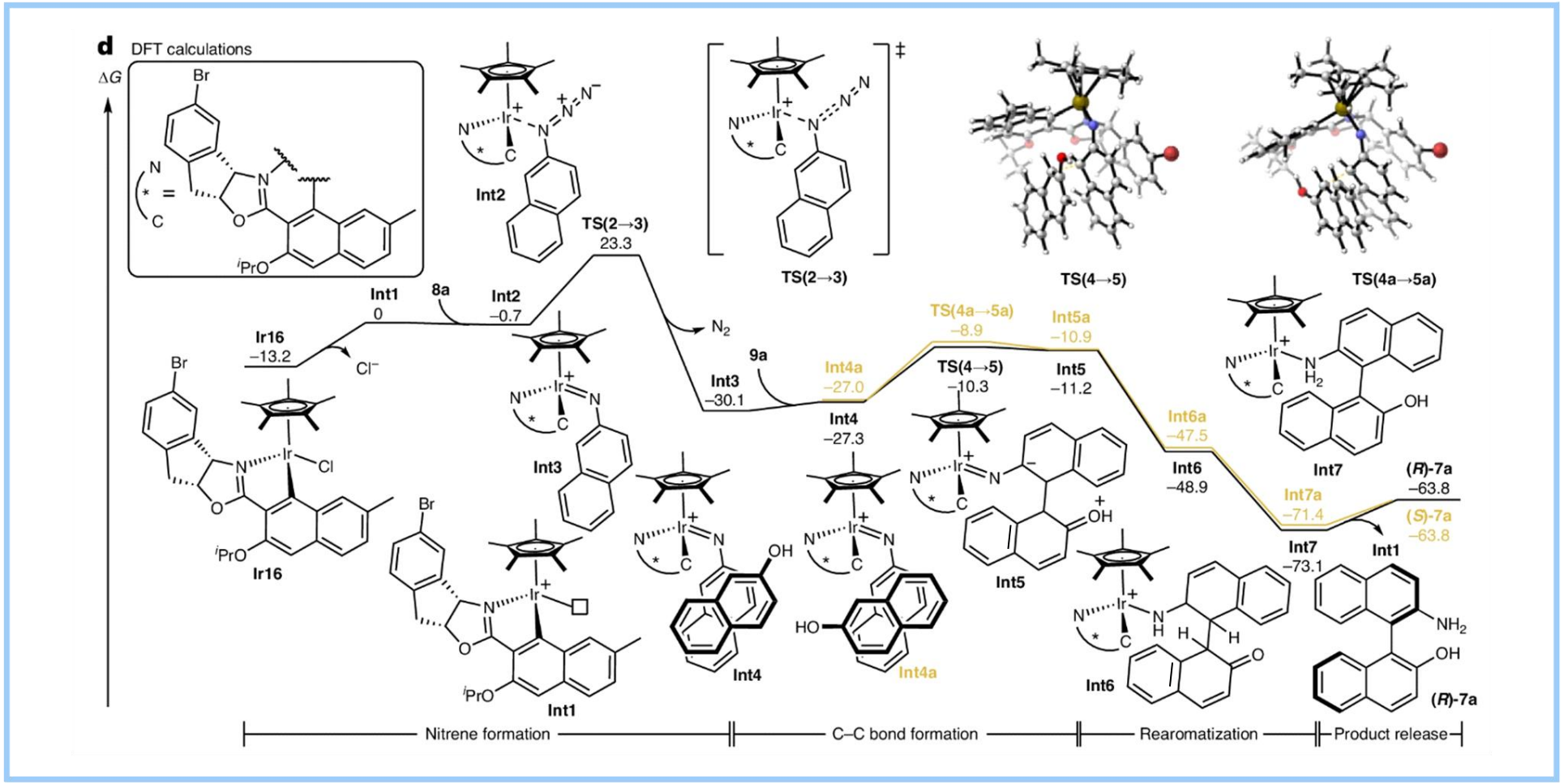
# Mechanism Study



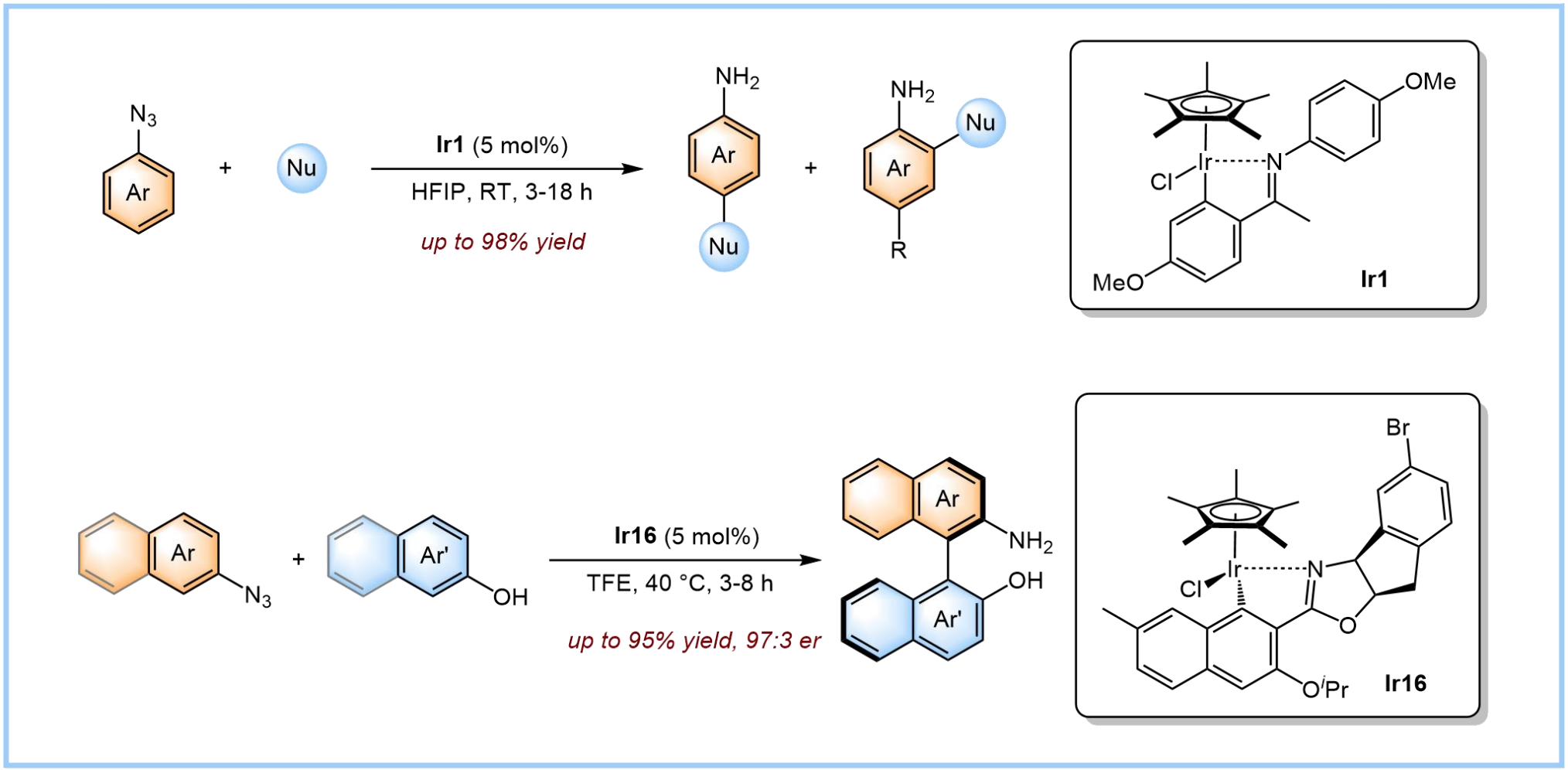
# Mechanism Study



# Mechanism Study



# Summary




**An iridium-catalysed site-selective and stereoselective arene C−H functionalization of readily available aryl azides with diverse nucleophiles has been developed.**

# The First Paragraph

## 写作思路

芳烃碳氢键官能化的重要性

↓

总结碳氢键官能化方法发展现状

↓

提出现有方法不足 引出本文工作

# The Last Paragraph

## 写作思路

总结工作：位点和立体选择性碳氢键官能化

↓

强调亮点：高对映选择性合成多种NOBINs

↓

提出展望：继续发展新的$S_NAr$反应

# Representative Examples

- In an interesting study, Hill, Maron and coworkers employed potent organocalcium nucleophiles and achieved nucleophilic alkylation of benzene. (potent: 强有力的，有影响力的)

- To start our investigation, we first examined the reaction of simple phenyl azide with various nucleophiles in the presence of metal complexes, to establish the feasibility of nitrene-mediated arene C−H functionalization via an $S_NAr$ pathway. (feasibility: 可行性；可能性)

- From a conceptual viewpoint, the above putative iridium nitrenoid-mediated C−H functionalization of phenyl azides represents a general strategy that should work for different arene azides, as well as various nucleophilic reaction partners. (conceptual: 概念的，观念的)

# Acknowledgment

***Thanks for your attention !***